Duehmke RM, Hollingshead J, Cornblath DR. Tramadol for neuropathic pain. (Review). Cochrane Database of Systematic Reviews 2006;Issue 3, Art # CD003726.

Design: Meta-analysis of randomized trials

PICOS:

- Population: patients with neuropathic pain of all ages and severity
- Intervention: any form of tramadol
- Comparison intervention: placebo or other pain relieving treatment
- Outcome: 50% or more pain relief
- Studies: randomized and quasi-randomized trials

Study search and selection:

- Electronic searches of MEDLINE, EMBASE, Cochrane Neuromuscular Disease Group Trials Register, and LILACS
- Two authors independently selected studies for inclusion, assessed methodological quality and study validity, resolving disagreements through discussion with the third author
- Methodological quality graded on the basis of allocation concealment and blinding of patient and observer

Results:

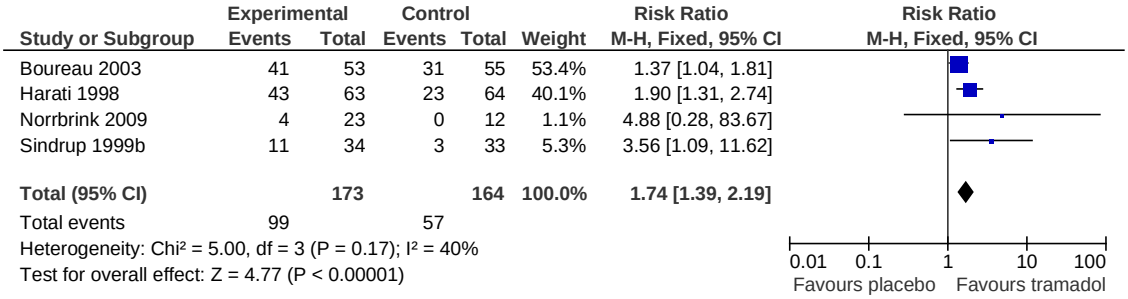
- 7 studies were identified as comparing tramadol with another intervention: 5 with placebo, 1 with clomipramine, and 1 with morphine
- Of the 5 trials comparing tramadol with placebo, none used 50% reduction in pain as the primary outcome measure, but 1 study used this as a secondary measure, and for two other studies, it was possible to calculate the proportion achieving 50% relief
- For 50% pain relief, the three studies which were pooled showed a relative benefit of tramadol over placebo of 1.70 under a fixed effect meta-analysis
- For side effects leading to withdrawal from the trial, the relative risk from two pooled studies was 5.37 under a fixed effect meta-analysis; the side effects included nausea, sweating, dry mouth, and sedation; all were reversible upon discontinuation of tramadol
- No conclusions could be drawn from the one trial comparing tramadol to morphine
- The trial comparing tramadol to the tricyclic antidepressant clomipramine was small and had methodological problems, and no conclusions were drawn from it

Authors' conclusions:

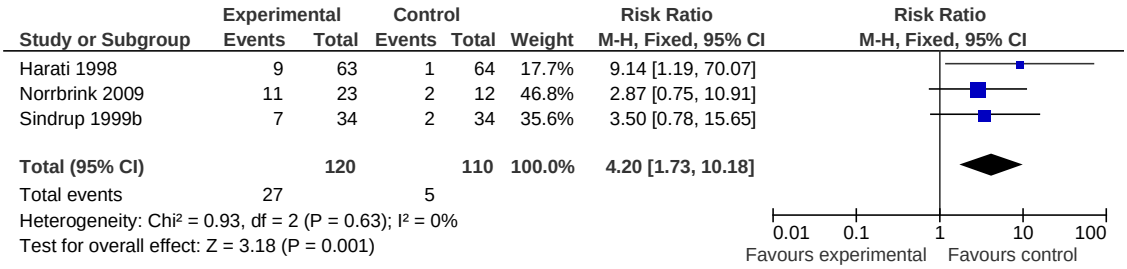
- Tramadol is an effective treatment for neuropathic pain
- Tramadol's efficacy is similar to that of antidepressants and anticonvulsants, but direct comparisons are not available
- Side effects may limit its use, but these are reversible and not life-threatening

Comments:

- Search strategy, information sources, description of study purpose, and selection and quality rating of articles are clearly described
- Search for unpublished material appears to be limited to the bibliographies of published trials and writing to study authors; publication bias issues not otherwise discussed
- Analysis 1.1, achievement of 50% pain relief, has a pooled risk ratio of 1.70 with the included studies; when Cochrane RevMan software is used to add Norrbrink 2009 to the forest plot, the risk ratio is unchanged at 1.74, and significant heterogeneity is not present



- Analysis 1.2, side effects leading to withdrawal, has a pooled risk ratio of 5.37; when the results of Norrbrink 2009 are added to the forest plot, the pooled risk ratio is 4.20



Assessment: adequate for evidence that tramadol alleviates neuropathic pain, but that adverse effects are frequent and may limit the usefulness of the drug (study would be higher quality if publication bias were addressed)